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EXAMINER

RAO, DEEPAK R

ART UNIT

PAPER NUMBER

1624

DATE MAILED: 09/24/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/975,741

Applicant(s)
Gaddam et al.

Examiner
Deepak Rao

Art Unit
1624



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Jul 8, 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-78 ☒ are pending in the application.
- 4a) Of the above, claim(s) 3-6, 12-26, and 35-77 ☒ are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 7-11, 27-34, and 78 ☒ are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 6 6) ☐ Other:

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DETAILED ACTION

Claims 1-78 are pending in this application.

Election/Restriction

Applicant's election with traverse of Group I, claims 1-2, 7-11, 27-34 and 78 in Paper No. 9 is acknowledged. The traversal is on the ground(s) that restriction between Groups I and III is improper and if the claims of Group I are found to be novel and non-obvious, then the use claims from Group III must be rejoined. This is not found persuasive because as explained in the previous office action, the methods of treating various diseases of the instant claims may be practiced by materially different products known in the art. Applicant's argument regarding rejoinder is fully considered, the use claims of Group III dependent on the product claims will be rejoined when the product is found to be allowable, following the procedure set forth in MPEP §821.04.

The requirement is still deemed proper and is therefore made FINAL.

Claims 3-6, 12-26 and 35-77 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

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Applicant's election of the species of Example 2 in paper no. 11 is acknowledged. The elected species represents a compound of formula (I) wherein X is S; R¹ and R² are H; n is 2; R³ is ethyl; and M is metformin.

The guidelines in MPEP § 803.02 provide that upon examination if prior art is found for the elected species, the examination will be limited to the elected species.

Content of MPEP § 803.02 is provided here for convenience:

As an example, in the case of an application with a Markush-type claim drawn to the compound C-R, wherein R is a radical selected from the group consisting of A, B, C, D and E, the examiner may require a provisional election of a single species, CA, CB, CC, CD or CE. The Markush-type claim would then be examined fully with respect to the elected species and any species considered to be clearly unpatentable over the elected species. If on examination the elected species is found to be anticipated or rendered obvious by prior art, the Markush-type claim and claims to the elected species shall be rejected, and claims to the non-elected species would be held withdrawn from further consideration. As in the prevailing practice, **a second action on the merits on the elected claims would be final.**

On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. **The prior art search, however, will not be extended unnecessarily to cover all nonelected species.** Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry.

The elected species was found in the prior art and as per the guidelines above, the search was limited to the elected species.

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Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11, 32, 33 and 34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of diabetes, does not reasonably provide enablement for treatment of all other diseases or **prevention** of the diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

The specification fails to enable one skilled in the art to use the claimed compounds. The use disclosed in the specification is as therapeutic agents having agonist activity against PPAR α and/or PPAR γ , useful in the treatment of various diseases, see pages 6-7. Test assays to measure PPAR agonist activity are provided at pages 25-26 and the results are provided for some of the exemplified compounds in a Table on page 26. This area of receptor activity is highly structure specific and unpredictable as can be seen from the range of the results obtained for the tested

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compounds. Further, there is no evidence on record which demonstrates that the *in-vitro* screening tests relied upon are recognized in the art as being reasonably predictive of success in any of the contemplated areas of regulating PPAR. Such a reasonable correlation is necessary to demonstrate such utilities. See *Ex parte Stevens*, 16 USPQ 2d 1379 (BPAI 1990); *Ex parte Busse et al.*, 1 USPQ 2d 1908 (BPAI 1986) (the evidence must be accepted as “showing” such utility, and not “warranting further study”). Fayer et al. (see the enclosed PubMed abstract) report that such correlation or lack thereof is important to predict drug-drug interactions such that no reasonable extrapolation could be made by one skilled in the art regarding the activity of the instantly claimed compounds. This clearly highlights the unpredictability in the art and the need for undue experimentation.

Further, the instantly claimed ‘conditions’ include “cancer” - no compound has ever been found to treat cancers of all types generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a “silver bullet” is contrary to our present understanding of oncology. Cecil Textbook of Medicine states that “each specific type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment and study” (see the enclosed article, page 1004). Different types of cancers affect different organs and have different methods of growth and harm to the body. Also see *In re Buting*, 163 USPQ 689 (CCPA 1969), wherein ‘evidence involving a single compound and two types of cancer, was held insufficient to establish the utility of the claims directed to disparate types of cancers’.

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The instant claims are drawn to 'A pharmaceutical composition for the treatment and/or **prevention**....' of several diseases, and therefore, the instant claim language embraces disorders not only for the treatment, but for "prevention" (or **prophylaxis**) which is not remotely enabled. Based on the selective PPAR receptor binding activity, the instant compounds are disclosed to be useful in the "prevention" of various diseases including diabetes, cardiovascular diseases, cancer, etc., for which applicants provide no competent evidence. "To prevent" actually means *to anticipate or counter in advance, to keep from happening etc.* (as per Webster's II Dictionary) and therefore it is not understood how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the 'prophylactic or preventive' effect. It is inconceivable from the *in vitro* data of a small number of representative compounds can be correlated to the 'treatment and **prevention or prophylaxis**' of the various claimed disorders, such that the claimed compounds can not only treat but also "prevent" a myriad of diseases associated with the stated activity. Further, there is no evidence on record which demonstrates that the *in-vitro* screening test relied upon is recognized in the art as being reasonably predictive of success in any of the contemplated areas of 'prevention'. Such a reasonable correlation is necessary to demonstrate such utilities.

The instant list of disorders includes conditions such as diabetes, for which it is conventionally known that there is no cure or prevention (see e.g., http://www.hutcheson.org/Services/diabetes/index_diabetes.htm). "Diabetes is a chronic disease that has **no cure**" according to American Diabetes Association (www.diabetes.org). The evidence presented in

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this case does not show such utilities related to 'prevention or prophylaxis', but only warrants further study. This clearly highlights the unpredictability in the art and the need for undue experimentation. Furthermore, there is no evidence of record which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disorders encompassed by the instant claims.

(Only a few of the claimed diseases are discussed here to make the point of an insufficient disclosure, it does not definitely mean that the other diseases meet the enablement requirements).

In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the claimed composition in the treatment and/or prevention of various diseases.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 7-11 and 27-34 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

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1. Claim 1 recites "Pharmaceutically acceptable **salts**..." in line 1, wherein the plural recitation in the preamble is not proper Markush language. Replacing the above with -- A pharmaceutically acceptable salt -- is suggested.
2. Claim 11 recites the limitation "A pharmaceutical composition as claimed in claim 8" in line 1. There is insufficient antecedent basis for this limitation in claim 8 on which claim 11 is dependent. Claim 8 recites "A composition" and the dependent claim should be written using consistent terminology. Same discrepancy is observed for claims 32-34 from their respective base claims.
3. Regarding claim 11, the phrase "such as" (see line 3) renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d). Claims 32-34 also have the same discrepancy.
4. In claim 11, line 4, it is not clear what is intended by "**other** cardiovascular disorders". It is not understood what 'other' cardiovascular disorders are included in the instant invention other than those that are those recited and the specification does not provide any help. Claims 32-34 also have same discrepancy.
5. In claims 11 and 32-34, the phrase "**including**", following 'certain renal diseases', renders the claims indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. Further, it is not clear if more diseases are intended by the recitation than those specified in the claim and what these diseases would be.

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Claims not particularly addressed above are included in the rejection because they are dependent claims and do not further resolve the above issues.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 8-11 and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Lohray et al., WO 99/20614. The instantly claimed salt form reads on the reference disclosed compound, see the compound of Example 30.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

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claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 7-11, 27-34 and 78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lohray et al., WO 99/20614. The reference teaches a generic group of compounds which embraces applicant's instantly claimed compounds. See formula (I) in page 8 and the various forms of pharmaceutically acceptable salts in page 15, lines 25-32. The compounds are taught to be useful as pharmaceutical therapeutic agents, see pages 1-2. The instant claims differ from the reference by reciting a specific species and/or specific salts that fall within the reference genus. It would have been obvious to one having ordinary skill in the art at the time of the invention to select any of the species of the genus taught by the reference, including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the species of the genus would have similar properties and, thus, the same use as taught for the genus as a whole i.e., as pharmaceutical therapeutic agents. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus. *In re Susi*, 440 F.2d 442, 169 USPQ 423, 425 (CCPA 1971), followed by

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the Federal Circuit in *Merck & Co. v. Biocraft Laboratories*, 847 F.2d 804, 10 USPQ 2d 1843, 1846 (Fed. Cir. 1989).

Duplicate Claims

Applicant is advised that should claim 8 be found allowable, claim 11 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 11 recites the intended use of the composition of claim 8 which is not given any patentable weight.

Applicant is advised that should claims 9, 27 and 28 be found allowable, claims 32, 33 and 34 will be objected to under 37 CFR 1.75 as being a substantial duplicates (respectively) thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). For example, claim 32 recites the intended use of the composition of claim 9 which is not given any patentable weight.

Receipt is acknowledged of the Information Disclosure Statement filed on October 10, 2001 and a copy is enclosed herewith.

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Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (703) 305-1879. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Mukund Shah, can be reached on (703) 308-4716. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.



**Deepak Rao
Primary Examiner
Art Unit 1624**

September 22, 2003